

Fig. 1

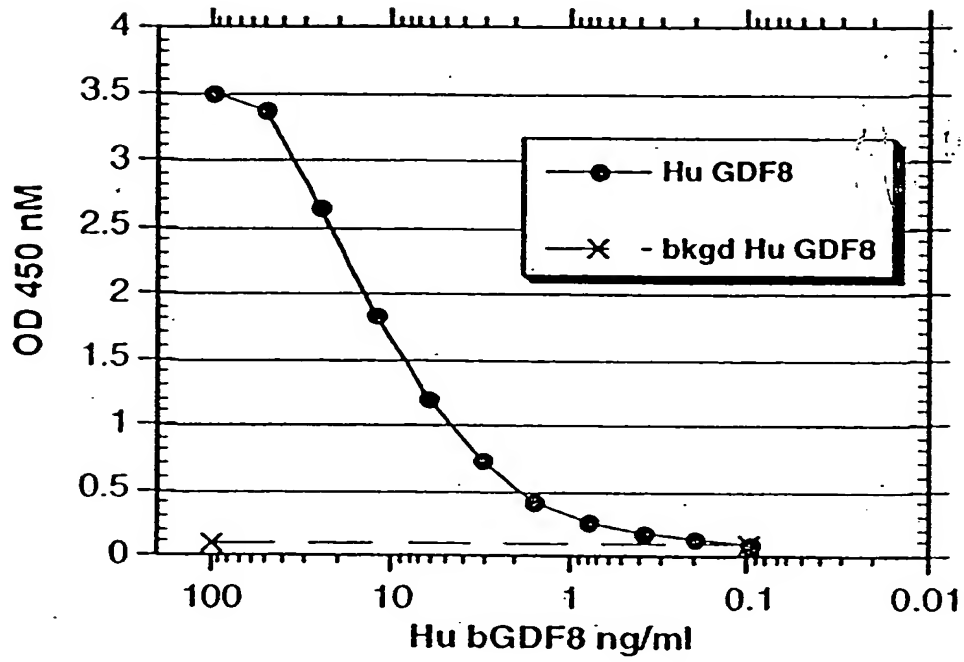


Fig. 2

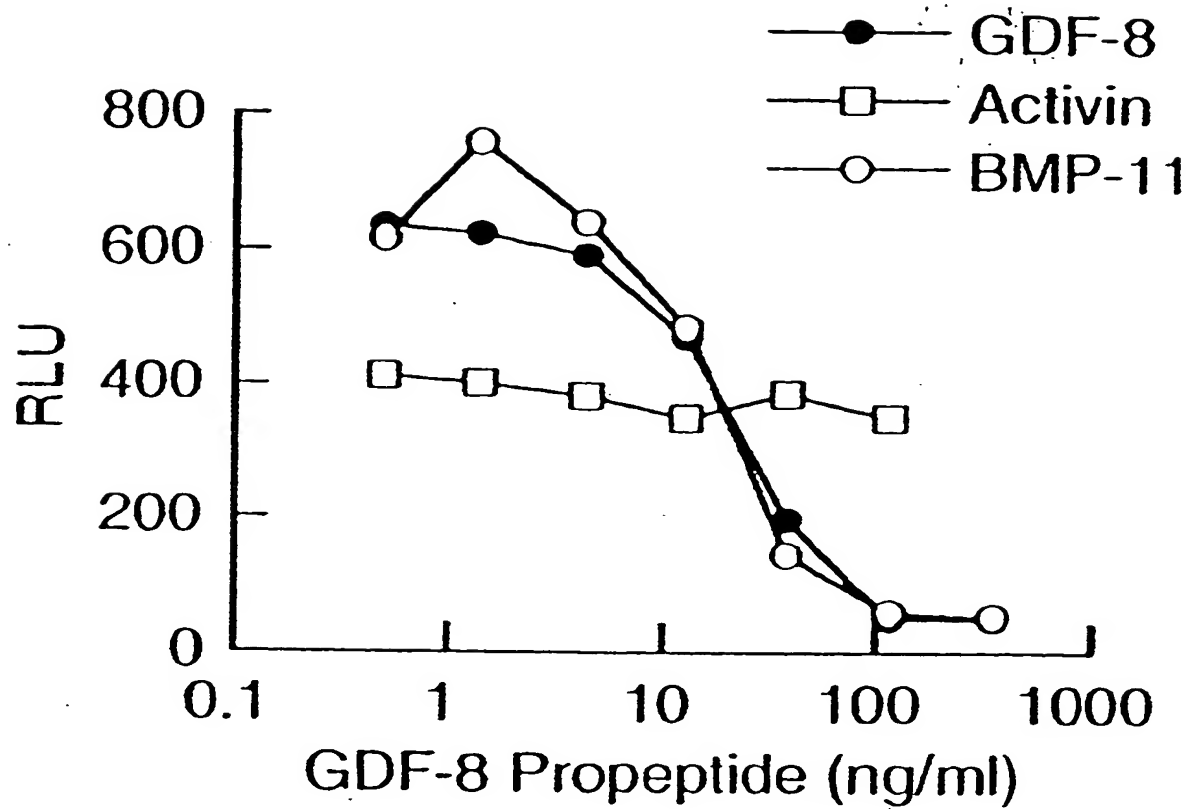


Fig. 3

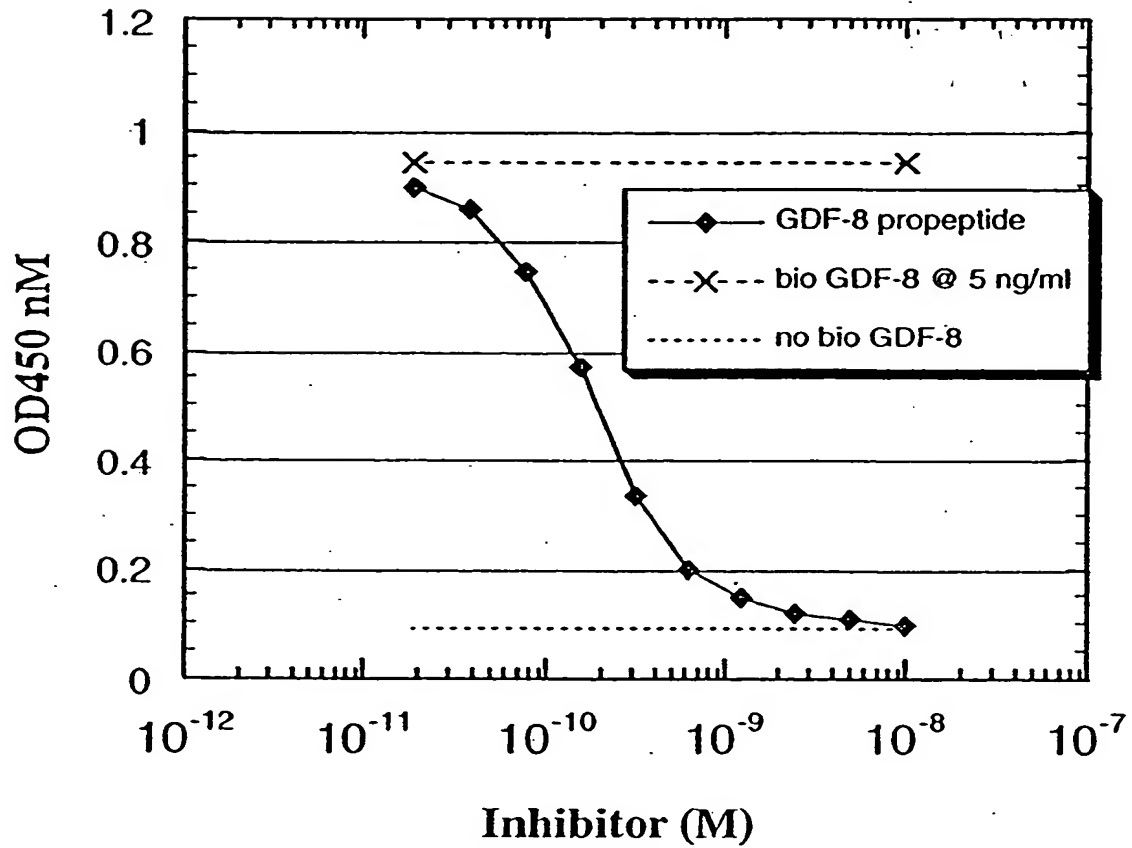


Fig. 4

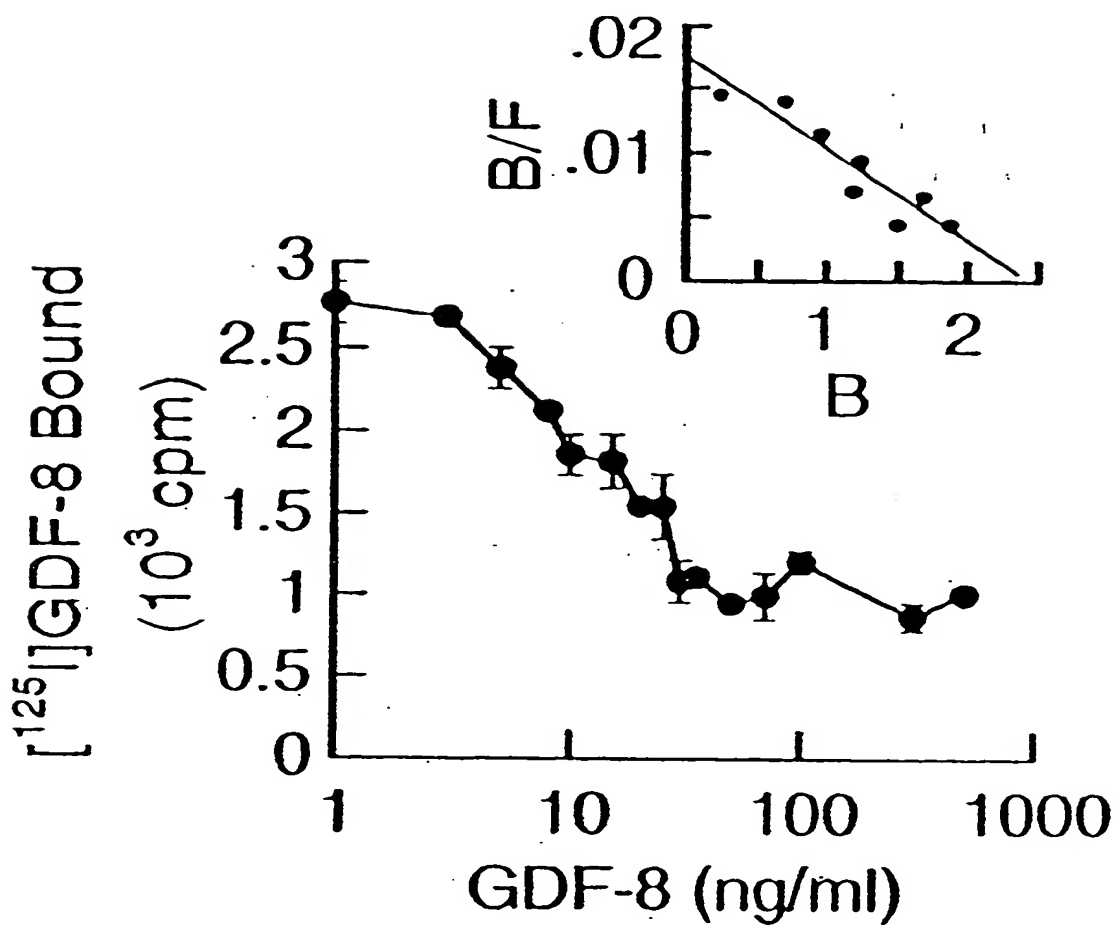


Fig. 5

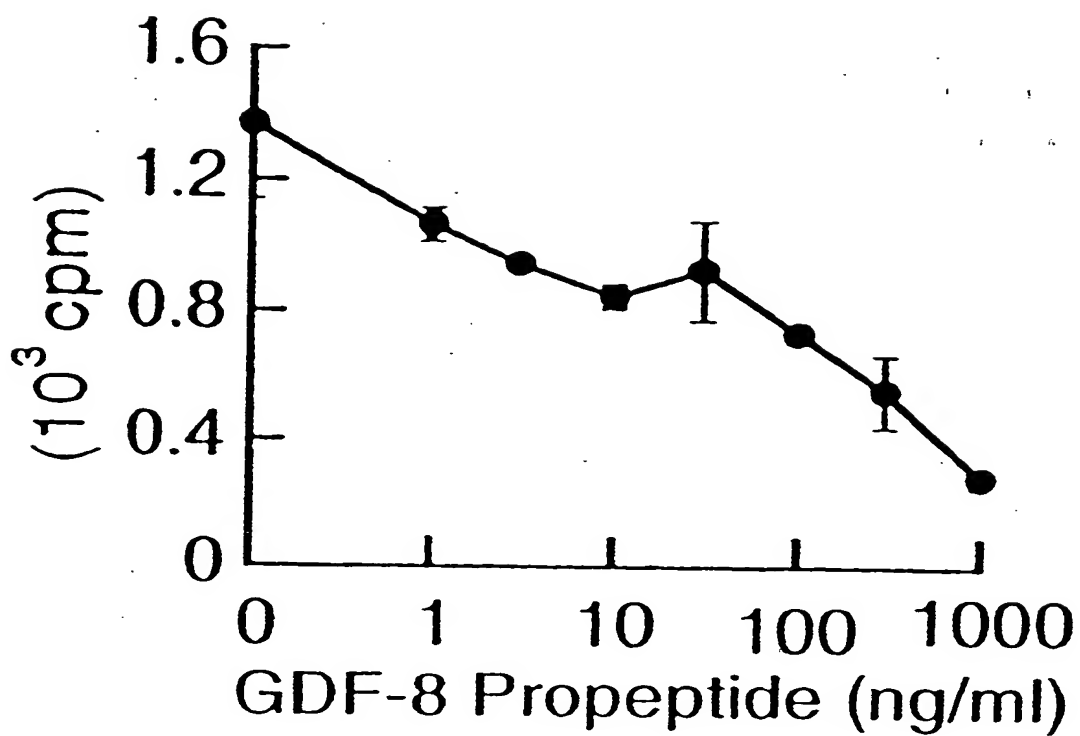


Fig. 6

NEGS	PKRS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc  
leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKIQLSKLRLET  
APNISKDAIRQLLPRAAPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQADGKPKC  
CFFKFSSKIQYNKVVAQQLWIYLRPVKTPTTVFVQILRLIKPMKDGTTRYTGIRSLKLDMSPGGTGIWQSI  
DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGPGEDGLNPFLEVKVTDTPKRSEPRGPTIKPCP  
PCKCPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWFFVNNVEVHTAQQTTHRE  
DYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQV  
TLTCMVTDMPEDIYVEWTNNGKTELNYKNTEPVLSDSGSYFMYSKLRVEKKNWVERNSYSCSVVHEGL  
HNHHTTKSFSRTPGK

Fig. 7A

NEGS	PKRS	GSGS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc  
leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKIQLSKLRLET  
APNISKDAIRQLLPRAAPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQADGKPKC  
CFFKFSSKIQYNKVVAQQLWIYLRPVKTPTTVFVQILRLIKPMKDGTTRYTGIRSLKLDMSPGGTGIWQSI  
DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGPGEDGLNPFLEVKVTDTPKRSGSGSEPRGPTI  
KPCPPCKCPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWFFVNNVEVHTAQQTQ  
THREDYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMT  
KKQVTLTCMVTDMPEDIYVEWTNNGKTELNYKNTEPVLSDSGSYFMYSKLRVEKKNWVERNSYSCSVV  
HEGLHNHHTTKSFSRTPGK

Fig. 7B

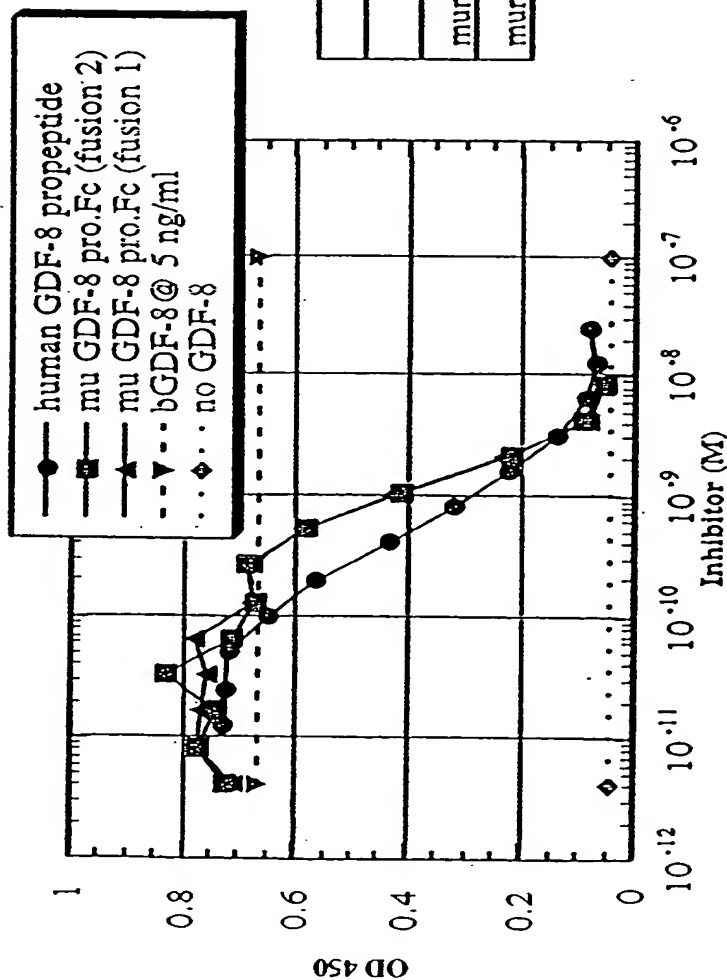


Fig. 8 A

Inhibitor	IC50 (M)
hu GDF-8 propeptide	$6 \times 10^{-10}$
murine GDF-8 pro.Fc (Fusion 1)	$1.3 \times 10^{-9}$
murine GDF-8 pro.Fc (Fusion 2)	$1.3 \times 10^{-9}$

Fig. 8 B



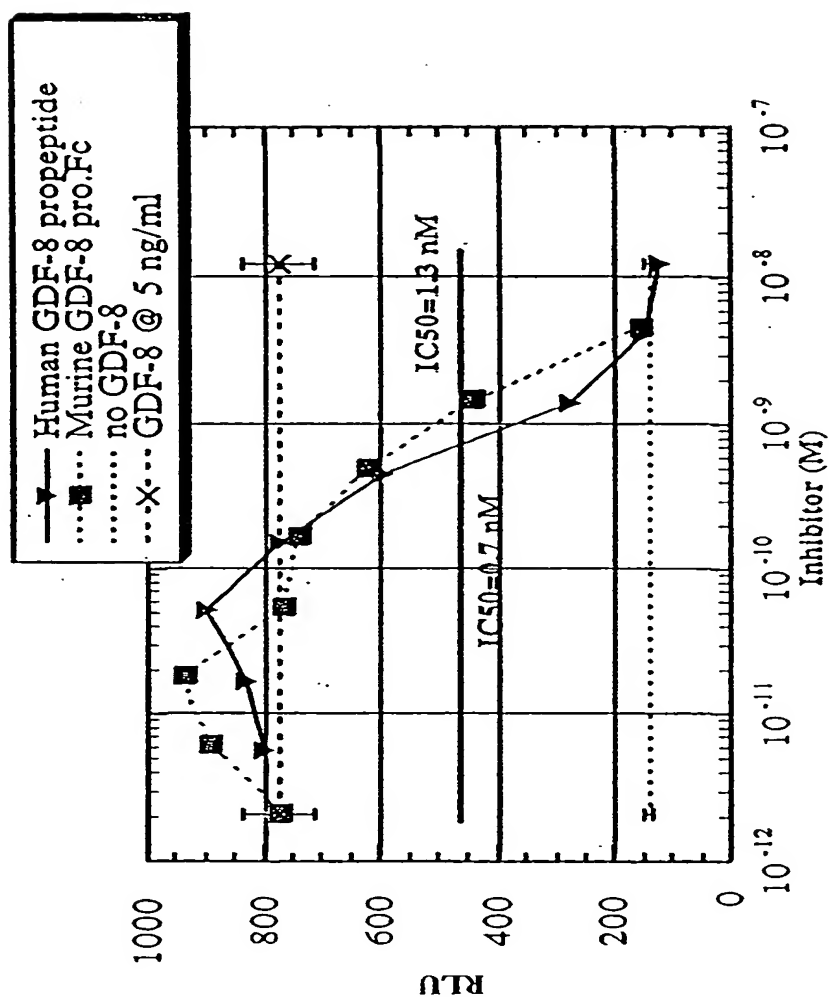


Fig. 9

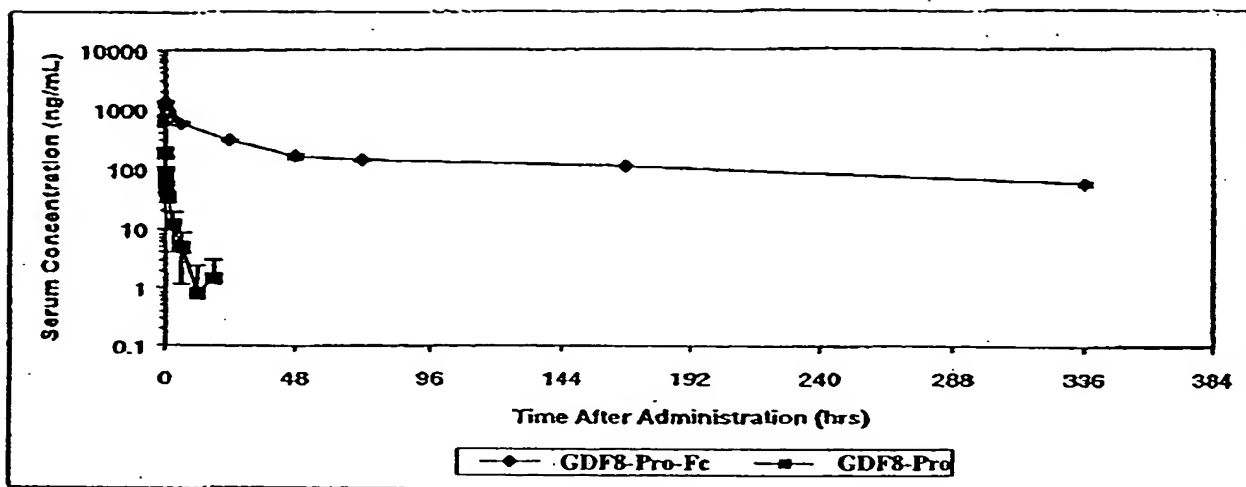


Fig. 10

Applicants: Neil M. Wolfman, *et al.*  
For: Modified and Stabilized GDF  
Propeptides and Uses Therefor  
Docket No.: AM100384

Secretory leader	Hu GDF-8 propeptide	Hu IgG1 Fc

MMQKLQLQCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN  
ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKF  
SSKIQYNKVVAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ  
NNWLKQPESNLGIEIKALDENGHDLAUTFPGGEDGLNPFLEVKVTDTPKRSEPKSCDKTHTCPPCPAPELL  
GGPSVFLFPPKPKD<sup>TM</sup>LSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL  
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDI  
AVEWESNGQPENNYKTTTPVLDS<sup>DS</sup>GSFFLYSKLTVDKSRWQQGNV<sup>FS</sup>CSVMHEALHNHYTQKSLSLSPGK

Fig. 11A

20080220 "6544200"

	NENS	PKRS	DKT	PGK
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Secretory      Hu GDF-8 propeptide      Hu IgG1 Fc mutated  
leader

MQKLQLCVYIYLFMLIVAGPVLDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN  
ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQVDGKPKCCFFKF  
SSKIQYNKVVKVKAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ  
NWLKQPESNLGIEIKALDENGHDLA VTFPGPGEDGLNPFLVVKVTDTPKRSDKTHTCPPCPAPEALGAPSV  
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNATKPREEQYNSTYRVVSVLTVHLQ  
DWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE  
SNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK

Fig. 11B

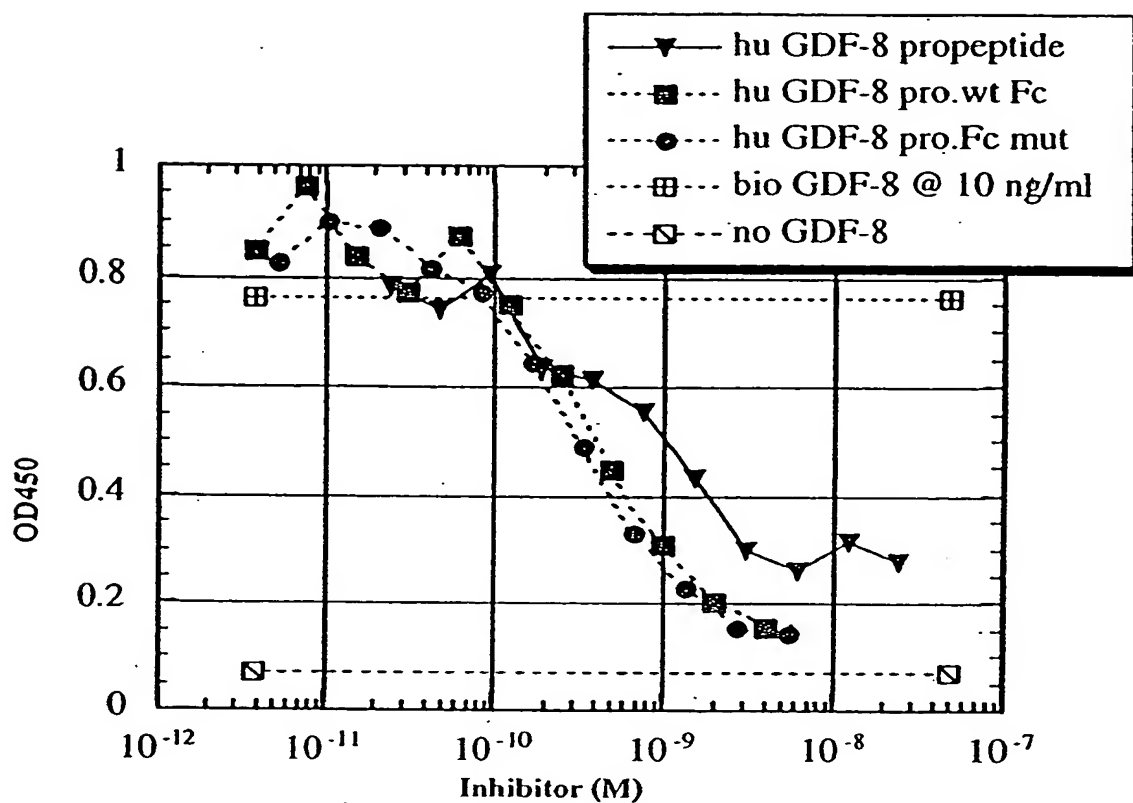


Fig. 12

## Dissected Tissue Mass

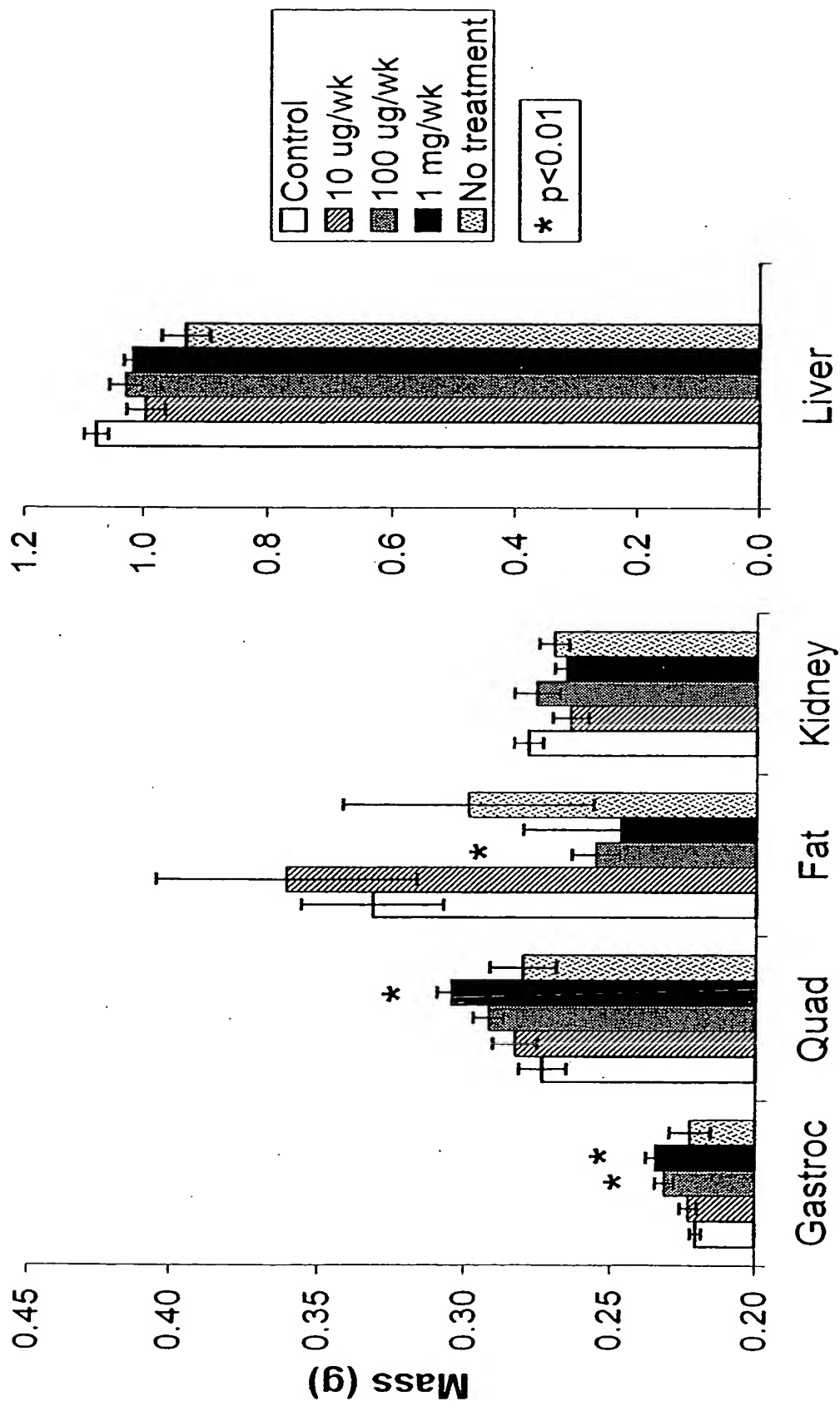


Figure 13

**Fig. 14A**

SEQ ID NO:1 Human GDF-8 precursor protein - protein  
sequence

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSS  
RIEAIKIQILSKLRLETAPNISKDVIRQLLPKAPPLRELIDQYDVQRDDSS  
DGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKFSSKIQYNKVVK  
AQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMNPGTGIWQ  
SIDVKTVLQNWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEV  
KVTDTPKRSRRDFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKA  
NYCSGECEFVFLQYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKE  
QIIYGKIPAMVVDRCGCS

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**Fig. 14B**

SEQ ID NO:2 Human GDF-8 precursor protein - DNA  
sequence

ATGCAAAAAGCTGCAACTCTGTGTTTATATTTACCTGTTTATGCTGATTGT  
TGCTGGTCCAGTGGATCTAAATGAGAACAGTGAGCAAAAAGAAAATGTGG  
AAAAAGAGGGGCTGTGTAATGCATGTACTTGGAGACAAAACACTAAATCT  
TCAAGAATAGAAGCCATTAAGATACAAATCCTCAGTAAACTTCGTCTGGA  
AACAGCTCCTAACATCAGCAAAGATGTTATAAGACAACCTTTTACCCAAAG  
CTCCTCCACTCCGGGAAGTATTGATCAGTATGATGTCCAGAGGGATGAC  
AGCAGCGATGGCTCTTTGGAAGATGACGATTATCACGCTACAACGGAAAC  
AATCATTACCATGCCTACAGAGTCTGATTTTCTAATGCAAGTGGATGGAA  
AACCCAAATGTTGCTTCTTTAAATTTAGCTCTAAAATACAATACAATAAA  
GTAGTAAAGGCCCAACTATGGATATATTTGAGACCCGTCGAGACTCCTAC  
AACAGTGTTTGTGCAAATCCTGAGACTCATCAAACCTATGAAAGACGGTA  
CAAGGTATACTGGAATCCGATCTCTGAAACTTGACATGAACCCAGGCACT  
GGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAAAATTGGCTCAA  
ACAACCTGAATCCAACCTTAGGCATTGAAATAAAAGCTTTAGATGAGAATG  
GTCATGATCTTGCTGTAACCTTCCCAGGACCAGGAGAAGATGGGCTGAAT  
CCGTTTTTTAGAGGTCAAGGTAACAGACACACCAAAAAGATCCAGAAGGGA  
TTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCGTT  
ACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCGCT  
CCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTATT  
TTTACAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCCAGAG  
GTTTCAGCAGGCCCTTGCTGTACTCCACAAAGATGTCTCCAATTAATATG  
CTATATTTTAATGGCAAAGAACAATAATATATGGGAAAATTCCAGCGAT  
GGTAGTAGACCGCTGTGGGTGCTCA



**Fig. 14C**

SEQ ID NO:3 Human mature GDF-8 - protein sequence

DFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGECEFVF  
LQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKEQIIYGKIPAMV  
VDRCGCS

**Fig. 14D**

SEQ ID NO:4 Human mature GDF-8 - DNA sequence

GATTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCG  
TTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCG  
CTCCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTA  
TTTTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCCAG  
AGGTTTCAGCAGGCCCTTGCTGTACTCCCACAAAGATGTCTCCAATTAATA  
TGCTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCG  
ATGGTAGTAGACCGCTGTGGGTGCTCA

**Fig.14E**

SEQ ID NO:5 Human GDF-8 propeptide - protein  
sequence

NENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPNISK  
DVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTES  
DFLMQVDGKPKCCFFKFSSKIQYNKVKAQLWIYLRPVETPTTVFVQILRL  
IKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQNLWKQPESNLGIEI  
KALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSRR

**Fig. 14F**

SEQ ID NO:6 Human GDF-8 propeptide - DNA sequence

AATGAGAACAGTGAGCAAAAAGAAAATGTGGAAAAAGAGGGGCTGTGTAAT  
GCATGTACTTGGAGACAAAACACTAAATCTTCAAGAATAGAAGCCATTAAG  
ATACAAATCCTCAGTAACTTCGTCTGGAAACAGCTCCTAACATCAGCAAA  
GATGTTATAAGACAACTTTTACCCAAAGCTCCTCCACTCCGGGAAGTGATT  
GATCAGTATGATGTCCAGAGGGATGACAGCAGCGATGGCTCTTTGGAAGAT  
GACGATTATCACGCTACAACGGAAACAATCATTACCATGCCTACAGAGTCT  
GATTTTCTAATGCAAGTGGATGGAAAACCCAAATGTTGCTTCTTTAAATTT  
AGCTCTAAAATACAATAACAATAAAGTAGTAAAGGCCCAACTATGGATATAT  
TTGAGACCCGTCGAGACTCCTACAACAGTGTTTGTGCAAATCCTGAGACTC  
ATCAAACCTATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAA  
CTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACA  
GTGTTGCAAAATTGGCTCAAACAACCTGAATCCAACCTTAGGCATTGAAATA  
AAAGCTTTAGATGAGAATGGTCATGATCTTGCTGTAACTTCCCAGGACCA  
GGAGAAGATGGGCTGAATCCGTTTTTAGAGGTCAAGGTAACAGACACACCA  
AAAAGATCCAGAAGG

**Fig. 14G**

SEQ ID NO:7 Human BMP-11 precursor protein -  
protein sequence

MVLAAPLLLGFLLLALELRPRGEAAEGPAAAAAAAAAAAAAGVGGERSRP  
APVAPEPDGCPVCVWRQHSRELRLSEIKSQILSKLRLKEAPNISREVVKQ  
LLPKAPPLQQIILDLHDFQGDALQPEDFLEEDEYHATTETVISMAQETDPAV  
QTDGSPLCCHFHFSPKVMFTKVLKAQLWVYLRPVPRPATVYLQILRLKPLT  
GEGTAGGGGGGRRHIRIRSLKIELHSRSGHWQSIDFKQVLHSWFRQPQSNW  
GIEINAFDPSGTDLAVTSLGPGAEGLHPFMELRVLENTKRSRRNLGLDCDE  
HSSESRCRYPLTVDFEAFGWDWI IAPKRYKANYCSGQCEYMFQMYPHTH  
LVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMVVDRCGCS

**Fig. 14H**

SEQ ID NO:8 Human BMP-11 precursor protein - DNA  
sequence

ATGGTGCTCGCGGCCCCGCTGCTGCTGGGCTTCCTGCTCCTCGCCCTGGA  
GCTGCGGCCCCGGGGGGAGGCGGCCGAGGGCCCCGCGGCGGCGGCGGCGG  
CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG  
CCAGCCCCGTCCGTGGCGCCCCGAGCCGGACGGCTGCCCCGTGTGCGTTTG  
GCGGCAGCACAGCCGCGAGCTGCGCCTAGAGAGCATCAAGTCGCAGATCT  
TGAGCAAACCTGCGGCTCAAGGAGGCGCCCAACATCAGCCGCGAGGTGGTG  
AAGCAGCTGCTGCCCAAGGCGCCGCGCTGCAGCAGATCCTGGACCTACA  
CGACTTCCAGGGCGACGCGCTGCAGCCCCGAGGACTTCCTGGAGGAGGACG  
AGTACCACGCCACCACCGAGACCGTCATTAGCATGGCCCAGGAGACGGAC  
CCAGCAGTACAGACAGATGGCAGCCCTCTCTGCTGCCATTTTCACTTCAG  
CCCCAAGGTGATGTTTACAAAGGTAAGGAGGAGGAGGAGGAGGAGGAGGAGG  
TACGGCCTGTACCCCGCCAGCCACAGTCTACCTGCAGATCTTGCGACTA  
AAACCCCTAACTGGGGAAGGGACCGCAGGGGGAGGGGGGCGGAGGCCGGCG  
TCACATCCGTATCCGCTCACTGAAGATTGAGCTGCACTCACGCTCAGGCC  
ATTGGCAGAGCATCGACTTCAAGCAAGTGCTACACAGCTGGTTCCGCCAG  
CCACAGAGCAACTGGGGCATCGAGATCAACGCCTTTGATCCCAGTGGCAC  
AGACCTGGCTGTACCTCCCTGGGGCCGGGAGCCGAGGGGCTGCATCCAT  
TCATGGAGCTTCGAGTCCTAGAGAACACAAAACGTTCCCGGCGGAACCTG  
GGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCGATATCC  
CCTCACAGTGGACTTTGAGGCTTTTCGGCTGGGACTGGATCATCGCACCTA  
AGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATGTTTCATG  
CAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAGAGGCTC  
TGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACATGCTCT  
ACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGCATGGTG  
GTGGATCGCTGTGGCTGCTCT

**Fig. 14I**

SEQ ID NO:9 Human BMP-11 mature - protein sequence

NLGLDCDEHSSESRCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMF  
MQKYPHTHLVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMV  
VDRCGCS

**Fig. 14J**

SEQ ID NO:10 Human BMP-11 mature - DNA sequence

AACCTGGGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCG  
ATATCCCCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCG  
CACCTAAGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATG  
TTCATGCAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAG  
AGGCTCTGCTGGGCCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACA  
TGCTCTACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGC  
ATGGTGGTGGATCGCTGTGGCTGCTCT

**Fig. 14K**

SEQ ID NO:11 Human BMP-11 propeptide - protein  
sequence

AEGPAAAAAAAAAAAAAGVGGERSSRPAPSVAPEPDGCPVCVWRQHSREL  
LESIKSQILSKLRLKEAPNISREVVKQLLPKAPPLQQILDLHDFQGDALQP  
EDFLEEDEYHATTETVISMAQETDPAVQTDGSPLCCHFHFSPKVMFTKVLK  
AQLWVYLRPVPRPATVYLLQILRLKPLTGEGTAGGGGGGRRHIRIRSLKIEL  
HSRSGHWQSIDFKQVLHWSFRQPQSNWGIEINAFDPSGTDLAVTSLGPGAE  
GLHPFMELRVLENTKRSRR

[illegible]

MQKLQLCVYIYLFMLIVAGPVDL

MVLAAPLLLGFLLLALELRPRGEA

**Fig. 14O**

SEQ ID NO:15 Human IgG1-Fc - protein sequence

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV  
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK  
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL  
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ  
GNVFSCSVMHEALHNHYTQKSLSLSPGK

**Fig. 14P**

SEQ ID NO:16 Human IgG1-Fc modified - protein  
sequence

DKTHTCPPCPAPEALGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP  
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK  
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY  
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS  
CSVMHEALHNHYTQKSLSLSPGK